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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,052	12/03/2004	Fatima Ferreira	966927.00048	5635

31496 7590 10/06/2008

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
10/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,052	FERREIRA ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,15,18 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,15,18 and 38* is/are rejected.

7)☒ Claim(s) *39-40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/25/2008 has been entered.

2. Claims 1, 4, 15, 18 and 38-40 are pending and currently under examination as they read on a polypeptide of SEQ ID NO:1 and a kit thereof.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 4, 15 and 18 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: an allergen consisting of SEQ ID NO:1; a polypeptide consisting of amino acids 181 to 396 of SEQ ID NO:1 and a polypeptide consisting of amino acids 21 to 180 of SEQ ID NO:1, a composition comprising the allergen and a kit thereof, does not provide reasonable enablement for: an isolated allergen consisting of a polypeptide capable of binding to IgE antibodies from an individual being allergic against mugwort pollen, wherein

said polypeptide is selected from the group consisting of : (a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 1; (b) **a polypeptide comprising the amino acid sequence extending between residues 21 and 180 of SEQ ID NO:1**; and (c) **a polypeptide comprising the amino acid extending between residues 181 and 396 of SEQ ID NO:1 of claim 1**; **wherein said polypeptide is further capable of binding to IgE antibodies from an individual being allergic against ragweed pollen** of claim 4; a **pharmaceutical composition** comprising the allergen as claimed in any one of claims 1 or 4 of claim 15; a kit for the diagnosis of an allergic disorder comprising the allergen as claimed in any one of claims 1 or 4 of claim 18. The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation for the same reasons as set forth in the Office Action mailed on 03/11/2008.

Applicant's arguments filed on 07/25/2008 and the 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues:

> "In this case, the instant specification clearly contemplates compositions comprising the allergenic sequence of the present invention in combination with other useful sequences. For example, at p. 8, lines 7-11 and p. 9, lines 24-31, Applicants expressly describe the inclusion of amino acid sequences which facilitate isolation and/or purification of the polypeptide of interest upon expression in a host cell, examples of which include a "6XHis tag, a FLAG tag, and sequences encoding bacterial proteins such as GST." Applicants respectfully submit that the manufacture of such heterologous fusion proteins is routine in the art of recombinant proteins. The present invention also contemplates pharmaceutical compositions comprised of the inventive allergens in combination with other therapeutically useful peptides, such as other allergenic peptides, synthetic epitopes, and adjuvants (see p. 11, line 29, to p. 12, line 10). Given the high level of skill in the art and the fact that a vast number of adjuvant and fusion constructs are presently known, and indeed conventional, in the art of peptide-based immunotherapy, the "trial and error" testing needed to identify suitable N-terminal or C-terminal additions is within the parameters of routine experimentation and optimization.

Furthermore, while it is well settled that the presence of some potentially inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled (see *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984)), Applicants respectfully submit that such potentially inoperative embodiments are excluded by the current claim language which requires that the allergen at issue bind to IgE antibodies from an individual being allergic against mugwort pollen, a function that is readily and routinely assayable using conventional techniques. See, for example, p. 4, lines 23-28. Thus, in that a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art, Applicants submit that one of ordinary skill in the art would be able to practice the invention of the presently pending claims without undue experimentation with a reasonable expectation of success.

With respect to claim 18, the Examiner continues to challenge the enablement of a kit for the *"prevention"* of an allergic disorder. While Applicants maintain that the Examiner's interpretation of the term "prevention" in the context of the present invention in unduly restrictive, Applicants have nevertheless canceled the term "prevention" from kit claim 18 to expedite prosecution. Thus, in that the present amendment to claim 18 renders moot the enablement rejection thereof, Applicants respectfully request reconsideration and withdrawal of the rejection.

With respect to claim 15, the Examiner continues to challenge the *in vivo* pharmaceutical efficacy of the claimed allergen peptide in the context of treating allergy, noting that allergens by definition bind IgE, thereby giving rise to allergy and anaphylaxis. The Examiner thus concludes that there is no reasonable correlation between a polypeptide that binds to IgE and an *in vivo* treatment method for allergies. Applicants respectfully disagree.

As noted on page 1 of the instant specification, it is nowadays widely accepted that recombinant allergens represent promising tools for diagnosis and therapy for Type I allergy. Peptide-based hypersensitization immunotherapy, whereby peptide agents bind cellular components of the immune system so as to suppress or densensitize the allergic response to particular allergens, is the gold standard for allergy treatment. Accordingly, allergen preparations are routinely made and administered for therapeutic purposes (e.g., to modify the allergic response of an allergen sensitive individual to a particular allergen). Purified allergen polypeptides and modified versions thereof may, for example, modify the B-cell response to an allergen, the T-cell response to an allergen or a combination of both. Purified allergens can also be used to design modified derivatives or analogues which are more useful in immunotherapy than are the unmodified, naturally-occurring peptides, such modified derivatives or analogues having the same or enhanced therapeutic properties with reduced side effects, especially reduced anaphylactic reactions. Accordingly, given the advanced state of the art of allergy therapy, Applicants respectfully submit that the *in vitro* data presented herein, data that demonstrates that the inventive polypeptides show clear and specific binding to mugwort pollen specific IgE antibodies, is sufficient to establish its utility in the context of allergy therapy.

Nevertheless, in an effort to expedite prosecution, Applicants submit herewith a declaration from Dr. Fatima Ferreira, including experimental data (Appendix A) that further confirms the pharmaceutical utility of the presently claimed allergens.

Numerous publications have shown that successful immunotherapy of allergic patients correlates with the modulation of allergen-specific T cells. Accordingly, a composition designed for allergen-specific immunotherapy should be able to address the existing T cells specific for the particular allergen to which the patient is allergic. These aspects are discussed in the review article by Larch et al. provided herewith as Appendix C (Larche, M. et al., "Immunological Mechanisms of Allergen-Specific Immunotherapy", *Immunology,* Vol. 6: 761-771, October 2006). As noted therein, in order to be successful, the allergy therapy should target the same T cell population that causes the development of the allergic reaction. However, through the inclusion of therapeutic adjuvants, these existing T cells will receive a "non-allergic" signal and will drive the immune response to the allergen in a "non-allergic" direction. This means the

synthesis of IgE antibodies will decrease and the IgG will increase, both due to different cytokines secreted by the T cells.

The stimulation index (SI) reflects the ability of an allergen or a peptide fragment thereof to activate T cells to proliferate. The SI is high when the allergen or peptide is added to the T cell culture and it is low when there is no allergen or peptide added. In order to distinguish background T cell proliferation from proliferation specifically induced by a peptide or by the intact allergen, Applicants set up a threshold value of 5. This means a reaction is considered positive (proliferation in response to the allergen) when the measured values of incorporated radioactivity is at least 5 times higher than the values in the T cell cultures without allergen/peptide added to the culture medium. As the data presented in the declaration provided herewith clearly demonstrate, the stimulation of peripheral blood mononuclear cells obtained from ragweed allergic individuals with the recombinant mugwort pollen allergen of the present invention (i.e., Art v 6 of SEQ ID NO: 1) induces proliferation of T cell lines at optimum concentrations (i.e., SI 4.3 to 11.2) as compared to that of non-allergic individuals (i.e., SI 1.5 to 4.2) and, as such, would be expected to have therapeutic utility in the context of allergen-specific immunotherapy. Thus, Applicants respectfully submit that the *in vitro* and *in vivo* data presented in the instant specification as well as the attached declaration demonstrate that a reasonable correlation exists between the scope of the claims and the scope of enablement. Accordingly, Applicants submit that one of ordinary skill in the art would be able to practice the invention of the presently pending claims without undue experimentation with a reasonable expectation of success. Therefore, Applicants respectfully request reconsideration and withdrawal of the enablement rejection of claim 15 in view of the amendments and remarks herein."

Page 5 of the specification teaches "the first one corresponding to beta chain spans amino acids 21 to 180 and the second one corresponding to alpha chain spans amino acids 181 to 396, both numberings referring to SEQ ID NO:1. Both chains are expected to have epitopes which are also present in the Amb a 1 chains resulting in the same IgE reactivity." However, the specification nor the post-dated art shows which regions of SEQ ID NO:1 are responsible for binding to IgE antibodies from an individual being allergic against mugwort or ragweed pollen. Without a correlation between the structure of SEQ ID NO:1 and the recited function of binding to IgE antibodies from an individual being allergic against mugwort or ragweed pollen, one of ordinary skill in the art would be required to perform undue experimentation to make and use the genus of polypeptides encompassed by the instant claim recitations directed to a polypeptide "comprising" the amino acid sequence extending between residues 21 and 180 of SEQ ID NO:1; and a polypeptide "comprising" the amino acid extending between residues 181 and 396 of SEQ

ID NO:1 of claim 1. The art of Lerner et al. teaches an antibody binding epitope may be as small as 6-15 amino acid residues (PTO-892, Reference U). Therefore, one of ordinary skill in the art would not know which core structure(s) of SEQ ID NO:1 are important for binding to IgE antibodies from an individual being allergic against mugwort or ragweed pollen without specific guidance.

The specification and 1.132 declaration filed by Fatima Ferreira are not sufficient to support the recitation of a pharmaceutical composition in claim 15. The in vitro T cell response data in Appendix A is not commensurate in scope with the claimed pharmaceutical composition. The Examiner finds no in vivo data in the specification, declaration or post-dated art to support the contention that the claims allergen can be used as in a pharmaceutical composition. The art of allergen immunotherapy as taught by Tarzi et al. (PTO-892; Reference V) teaches that whole allergen immunotherapy is unpredictable due to the retention of B-cell epitopes within the allergen which confers a risk of IgE-mediated potentially life-threatening systemic reactions (In particular, paragraph spanning pages 617-618, whole document) In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical compositions are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

5. Claims 1, 4, 15 and 18 stand rejected under 35 U.S.C. 112, first paragraph, as

containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons as set forth in the Office Action mailed on 03/11/2008.

Applicant's arguments and 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues:

> "In this case, Applicants respectfully disagree with the Examiner's position and submit her conclusions are in conflict with the recently promulgated Revision 1 of the Written Description Training Materials published March 25, 2008.. particularly Examples 4 and 15, both of which validate the use of open-language in this context. In assessing adequacy of written description, the examples expressly conclude that it is within the level of skill and knowledge in the art to add any desired DNA sequence to either end of a particular sequence, with no more than routine experimentation. Because the claimed sequence is a structural feature common to members of the claimed genus and the specification describes the complete structure (sequence) of the molecule, one skilled in the art would recognize that the applicant was in possession of a structural feature shared by members of the claimed genus. Accordingly, the species disclosed in the specification; *i.e.,* SEQ ID NO: 1 and the functional fragments thereof, are sufficiently representative of the claimed genus and thus the written description requirement of 35 U.S.C. 112, first paragraph, is satisfied.
>
> Thus, Applicants respectfully submit that the instant specification provides an adequate written description of the genus of allergens encompassed by claims 1 *et seq.,* so as to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicants were in possession of the invention now claimed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the written description rejection of claims 1, 3, 4, 15, 18, 20, and 38-40 in view of the amendments and remarks herein."

It is the Examiner's position that Example 11 of the Written Description Training

Materials published March 25, 2008 is the appropriate reference for guidance in the instant case. The fragments of a full-disclosed polypeptide are likened to percent identity of a fully disclosed polypeptide. It is the Examiner's position that the specification does not disclose a correlation between the structure of the allergen fragments "comprising the amino acid sequence extending between residues 21 and 180 of SEQ ID NO:1" and "comprising the amino acid extending between residues 181 and 396 of SEQ ID NO:1" and the function (capable of binding to IgE antibodies from an individual being allergic against mugwort pollen or ragweed pollen) such that a skilled artisan would have known what allergens comprising the fragments of SEQ ID NO:1 possess the claimed function. "Possession may not be shown by merely describing how to obtain possession of member of the claimed genus or how to identify their common structural features" *Ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)) at page 16. In this instant case Applicants have not provided any guidance as to what core structures of SEQ ID NO:1 will result in the claimed functions of binding to IgE from an individual allergic to mugwort or ragweed pollen. It is noted that there is no disclosure in the specification that both fragments possess the recited functions. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra*, at page 17. In the instant case, definition by function does not suffice to define the genus because it is only an indication of what the allergen does rather than what it is.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 4 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nilsen et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 03/11/2008.

Applicant's arguments and 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues

"Applicants not only disagree with the Examiner's characterization of the prior art disclosures but also submit that the Examiner has erroneously placed the burden on Applicants to "prove" that the claimed allergen is distinct from the peptide of the prior art. Applicants reiterate that it is not their burden to demonstrate uniqueness but instead the Examiner's burden to demonstrate anticipation. Thus, it is improper to demand that Applicants "prove" that the various "approximately 40.9 kDa" mugwort pollen extracts of the prior art are different from that which is presently claimed, particularly when Applicants have previously presented ample evidence suggestive of distinction (e.g. differences in measurable parameters such as MW, pI, amino acid composition, etc.) and more recently accumulated evidence that casts doubt on the Examiner's suggestion that Applicants' SEQ ID NO: 1 is "more likely than not" to be among the mugwort pollen extracts identified in the prior art (see Appendix B of the attached declaration). Specifically, as the data provided herewith as Appendix B demonstrates, several potentially allergenic proteins within the range of 40-44 kDa band coexist in mugwort pollen extract.

As noted previously, the suggestion that a certain result or characteristic occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Likewise, the fact that an event ~ result from a given set of circumstances is not sufficient to establish anticipation. *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Under the principle of inherency, anticipation may not be established by probabilities or possibilities ("A prior art event cannot be established based on speculation, or where a doubt exists." *Ethyl Molded Product Co. v. Betts Package, Inc.,* 9 USPQ 2d 1001, 1032-33 (E.D.KY 1988). Rather, the doctrine of inherency is available only when the prior inherent event can be established with certainty. Thus, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Accordingly, when relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent

characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

In this case, Applicants previously presented evidence that the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. were not identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Applicants herewith present further evidence establishing that the reference proteins could be any one of a number of extract proteins (See Appendix B). Thus, Applicants respectfully submit that since one cannot be certain that the claimed peptide is necessarily present in any of the references, the references cannot anticipate the invention of the pending claims.

In sum, Applicants respectfully submit that none of the polypeptides described in the prior art are identical to the presently claimed ~40.9 kDa Art v 6 protein defined in SEQ ID NO: 1. Since the cited prior art references fail to explicitly or inherently suggest each and every claimed element, Applicants submit that they cannot anticipate the invention of the pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the anticipation rejections of claim 1, 4, 15, 18, and 38 in view of the amendments and remarks herein.. "

It remains the Examiner's position that Nilsen et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, Figure 1, approximately 44 kDa bands in lanes C, E, F and K; Table 1, whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa bands of Figure 1 in Nilsen et al. are the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant has not met their burden to show that the allergen in Nilsen et al. is not the allergen of SEQ ID NO:1 by saying that it is not necessarily the same allergen since it could have been any one of the allergens found in Appendix B submitted in the declaration of Fatima Ferreria on 07/25/2008. No sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6, but on the other hand no information has been provided to unequivocally prove that the isolated protein of Nilsen is not the recited Art v 1 of SEQ ID NO:1. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. Further, it is noted that the proteins set forth in Appendix B of the declaration filed of Fatima Ferreira filed on 07/25/2008 were not isolated using IgE or serum of mugwort pollen allergic patients. Therefore, Applicant has not provided data to suggest that there are any other proteins of that size that are recognized by mugwort-pollen allergic patients as described in Nilsen et al. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

8. Claims 1, 4 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Brandys et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 03/11/2008.

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" Applicants not only disagree with the Examiner's characterization of the prior art disclosures but also submit that the Examiner has erroneously placed the burden on Applicants to "prove" that the claimed allergen is distinct from the peptide of the prior art. Applicants reiterate that it is not their burden to demonstrate uniqueness but instead the Examiner's burden to demonstrate anticipation. Thus, it is improper to demand that Applicants "prove" that the various "approximately 40.9 kDa" mugwort pollen extracts of the prior art are different from that which is presently claimed, particularly when Applicants have previously presented ample evidence suggestive of distinction (e.g. differences in measurable parameters such as MW, pI, amino acid composition, etc.) and more recently accumulated evidence that casts doubt on the Examiner's suggestion that Applicants' SEQ ID NO: 1 is "more likely than not" to be among the mugwort pollen extracts identified in the prior art (see Appendix B of the attached declaration). Specifically, as the data provided herewith as Appendix B demonstrates, several potentially allergenic proteins within the range of 40-44 kDa band coexist in mugwort pollen extract.

As noted previously, the suggestion that a certain result or characteristic occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Likewise, the fact that an event ~ result from a given set of circumstances is not sufficient to establish anticipation. *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Under the principle of inherency, anticipation may not be established by probabilities or possibilities ("A prior art event cannot be established based on speculation, or where a doubt exists." *Ethyl Molded Product Co. v. Betts Package, Inc.,* 9 USPQ 2d 1001, 1032-33 (E.D.KY 1988). Rather, the doctrine of inherency is available only when the prior inherent event can be established with certainty. Thus, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Accordingly, when relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

In this case, Applicants previously presented evidence that the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. were not identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Applicants herewith present further evidence establishing that the reference proteins could be any one of a number of extract proteins (See Appendix B). Thus, Applicants respectfully submit that since one cannot be certain that the claimed peptide is necessarily present in any of the references, the references cannot anticipate the invention of the pending claims.

In sum, Applicants respectfully submit that none of the polypeptides described in the prior art are identical to the presently claimed ~40.9 kDa Art v 6 protein defined in SEQ ID NO: 1. Since the cited prior art references fail to explicitly or inherently suggest each and every claimed element, Applicants submit that they cannot anticipate the invention of the pending claims. Accordingly, Applicants respectfully

request reconsideration and withdrawal of the anticipation rejections of claim 1, 4, 15, 18, and 38 in view of the amendments and remarks herein."

It remains the Examiner's position that Brandys et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, Figure 2C, approximately 44 kDa band in lanes v, c, s, p, whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa bands of Figure 2C in Brandys et al. are the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant has not met their burden to show that the allergen in Brandys et al. is not the allergen of SEQ ID NO:1 by saying that it is not necessarily the same allergen since it could have been any one of the allergens found in Appendix B submitted in the declaration of Fatima Ferreria on 07/25/2008. No sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6, but on the other hand no information

has been provided to unequivocally prove that the isolated protein of Brandys is not the recited Art v 1 of SEQ ID NO:1. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. Further, it is noted that the proteins set forth in Appendix B of the declaration filed of Fatima Ferreira filed on 07/25/2008 were not isolated using IgE or serum of mugwort pollen allergic patients. Therefore, Applicant has not provided data to suggest that there are any other proteins of that size that are recognized by mugwort-pollen allergic patients as described in Brandys et al. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

9. Claims 1, 4 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hirschwehr et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 03/11/2008.

Applicant's arguments and 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues

> " Applicants not only disagree with the Examiner's characterization of the prior art disclosures but also submit that the Examiner has erroneously placed the burden on Applicants to "prove" that the claimed

allergen is distinct from the peptide of the prior art. Applicants reiterate that it is not their burden to demonstrate uniqueness but instead the Examiner's burden to demonstrate anticipation. Thus, it is improper to demand that Applicants "prove" that the various "approximately 40.9 kDa" mugwort pollen extracts of the prior art are different from that which is presently claimed, particularly when Applicants have previously presented ample evidence suggestive of distinction (e.g. differences in measurable parameters such as MW, pI, amino acid composition, etc.) and more recently accumulated evidence that casts doubt on the Examiner's suggestion that Applicants' SEQ ID NO: 1 is "more likely than not" to be among the mugwort pollen extracts identified in the prior art (see Appendix B of the attached declaration). Specifically, as the data provided herewith as Appendix B demonstrates, several potentially allergenic proteins within the range of 40-44 kDa band coexist in mugwort pollen extract.

As noted previously, the suggestion that a certain result or characteristic occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Likewise, the fact that an event ~ result from a given set of circumstances is not sufficient to establish anticipation. *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Under the principle of inherency, anticipation may not be established by probabilities or possibilities ("A prior art event cannot be established based on speculation, or where a doubt exists." *Ethyl Molded Product Co. v. Betts Package, Inc.,* 9 USPQ 2d 1001, 1032-33 (E.D.KY 1988). Rather, the doctrine of inherency is available only when the prior inherent event can be established with certainty. Thus, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Accordingly, when relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

In this case, Applicants previously presented evidence that the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. were not identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Applicants herewith present further evidence establishing that the reference proteins could be any one of a number of extract proteins (See Appendix B). Thus, Applicants respectfully submit that since one cannot be certain that the claimed peptide is necessarily present in any of the references, the references cannot anticipate the invention of the pending claims.

In sum, Applicants respectfully submit that none of the polypeptides described in the prior art are identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1. Since the cited prior art references fail to explicitly or inherently suggest each and every claimed element, Applicants submit that they cannot anticipate the invention of the pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the anticipation rejections of claim 1, 4, 15, 18, and 38 in view of the amendments and remarks herein. "

It remains the Examiner's position that Hirschwehr et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, approximately 44kDa bands in Figure 1A, bands in lanes 10, 11 and 13; Figure 3A,

lanes 6 and 7; and Figure 5, patients A and B; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa bands of Figures 1A, 3A and 5 in Hirschwehr et al. are the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant has not met their burden to show that the allergen in Hirschwehr et al. is not the allergen of SEQ ID NO:1 by saying that it is not necessarily the same allergen since it could have been any one of the allergens found in Appendix B submitted in the declaration of Fatima Ferreria on 07/25/2008. No sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6, but on the other hand no information has been provided to unequivocally prove that the isolated protein of Hirschwehr is not the recited Art v 1 of SEQ ID NO:1. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. Further, it is

noted that the proteins set forth in Appendix B of the declaration filed of Fatima Ferreira filed on 07/25/2008 were not isolated using IgE or serum of mugwort pollen allergic patients. Therefore, Applicant has not provided data to suggest that there are any other proteins of that size that are recognized by mugwort-pollen allergic patients as described in Hirschwehr et al. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument are not sufficient to overcome the rejection.

10. Claims 1, 4 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by De La Hoz et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 03/11/2008.

Applicant's arguments and 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues:

> " Applicants not only disagree with the Examiner's characterization of the prior art disclosures but also submit that the Examiner has erroneously placed the burden on Applicants to "prove" that the claimed allergen is distinct from the peptide of the prior art. Applicants reiterate that it is not their burden to demonstrate uniqueness but instead the Examiner's burden to demonstrate anticipation. Thus, it is improper to demand that Applicants "prove" that the various "approximately 40.9 kDa" mugwort pollen extracts of the prior art are different from that which is presently claimed, particularly when Applicants have previously presented ample evidence suggestive of distinction (e.g. differences in measurable parameters such as MW, pI, amino acid composition, etc.) and more recently accumulated evidence that casts doubt on the Examiner's suggestion that Applicants' SEQ ID NO: 1 is "more likely than not" to be among the mugwort pollen extracts identified in the prior art (see Appendix B of the attached declaration). Specifically, as the data provided herewith as Appendix B demonstrates, several potentially allergenic proteins within the range of 40-44 kDa band coexist in mugwort pollen extract.

> As noted previously, the suggestion that a certain result or characteristic occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Likewise, the fact that an event ~ result from a given set of circumstances is not sufficient to establish anticipation. *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Under the principle of inherency, anticipation may not be established by probabilities or possibilities ("A prior art event cannot be established based on speculation, or where a doubt exists." *Ethyl Molded Product Co. v. Betts Package, Inc.,* 9 USPQ 2d 1001, 1032-33 (E.D.KY 1988). Rather, the doctrine of inherency is available only when the prior inherent event can be established with certainty. Thus, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Accordingly, when relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).
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> In this case, Applicants previously presented evidence that the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. were not identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Applicants herewith present further evidence establishing that the reference proteins could be any one of a number of extract proteins (See Appendix B). Thus, Applicants respectfully submit that since one cannot be certain that the claimed peptide is necessarily present in any of the references, the references cannot anticipate the invention of the pending claims.
>
> In sum, Applicants respectfully submit that none of the polypeptides described in the prior art are identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1. Since the cited prior art references fail to explicitly or inherently suggest each and every claimed element, Applicants submit that they cannot anticipate the invention of the pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the anticipation rejections of claim 1, 4, 15, 18, and 38 in view of the amendments and remarks herein.. "

It remains the Examiner's position that De La Hoz et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, approximately 44kDa bands in Figure 3, lanes A and B, Figure 4, lanes A, B and C; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore,

absent evidence to the contrary, the approximately 44 kDa bands of Figure 3 in De La Hoz et al. are the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant has not met their burden to show that the allergen in De La Hoz et al. is not the allergen of SEQ ID NO:1 by saying that it is not necessarily the same allergen since it could have been any one of the allergens found in Appendix B submitted in the declaration of Fatima Ferreria on 07/25/2008. No sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6, but on the other hand no information has been provided to unequivocally prove that the isolated protein of De La Hoz is not the recited Art v 1 of SEQ ID NO:1. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. Further, it is noted that the proteins set forth in Appendix B of the declaration filed of Fatima Ferreira filed on 07/25/2008 were not isolated using IgE or serum of mugwort pollen allergic patients. Therefore, Applicant has not provided data to suggest that there are any other proteins of that size that are recognized by mugwort-pollen allergic patients as described in De La Hoz et al. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument are not sufficient to overcome the rejection.

11. Claims 1, 4 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Katial et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 03/11/2008.

Applicant's arguments and 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues:

> " Applicants not only disagree with the Examiner's characterization of the prior art disclosures but also submit that the Examiner has erroneously placed the burden on Applicants to "prove" that the claimed allergen is distinct from the peptide of the prior art. Applicants reiterate that it is not their burden to demonstrate uniqueness but instead the Examiner's burden to demonstrate anticipation. Thus, it is improper to demand that Applicants "prove" that the various "approximately 40.9 kDa" mugwort pollen extracts of the prior art are different from that which is presently claimed, particularly when Applicants have previously presented ample evidence suggestive of distinction (e.g. differences in measurable parameters such as MW, pI, amino acid composition, etc.) and more recently accumulated evidence that casts doubt on the Examiner's suggestion that Applicants' SEQ ID NO: 1 is "more likely than not" to be among the mugwort pollen extracts identified in the prior art (see Appendix B of the attached declaration). Specifically, as the data provided herewith as Appendix B demonstrates, several potentially allergenic proteins within the range of 40-44 kDa band coexist in mugwort pollen extract.
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> As noted previously, the suggestion that a certain result or characteristic occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Likewise, the fact that an event ~ result from a given set of circumstances is not sufficient to establish anticipation. *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Under the principle of inherency, anticipation may not be established by probabilities or possibilities ("A prior art event cannot be established based on speculation, or where a doubt exists." *Ethyl Molded Product Co. v. Betts Package, Inc.,* 9 USPQ 2d 1001, 1032-33 (E.D.KY 1988). Rather, the doctrine of inherency is available only when the prior inherent event can be established with certainty. Thus, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Accordingly, when relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

> In this case, Applicants previously presented evidence that the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. were not identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Applicants herewith present further evidence establishing that the reference proteins could be any one of a number of extract proteins (See Appendix B). Thus, Applicants respectfully submit that since one cannot be certain that the claimed peptide is necessarily present in any of the references, the references cannot anticipate the invention of the pending claims.
>
> In sum, Applicants respectfully submit that none of the polypeptides described in the prior art are identical to the presently claimed ~40.9 kDa Art v 6 protein defined in SEQ ID NO: 1. Since the cited prior art references fail to explicitly or inherently suggest each and every claimed element, Applicants submit that they cannot anticipate the invention of the pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the anticipation rejections of claim 1, 4, 15, 18, and 38 in view of the amendments and remarks herein.. "

It remains the Examiner's position that Katial et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, Figure 5, approximately 44kDa band in lane AV; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa band of Figure 5 in Katial et al. is the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant has not met their burden to show that the allergen in Katial et al. is not the allergen of SEQ ID NO:1 by saying that it is not necessarily the same allergen since it could have been any one of the allergens found in Appendix B submitted in the declaration of Fatima Ferreria on 07/25/2008. No sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6, but on the other hand no information has been provided to unequivocally prove that the isolated protein of Katial is not the recited Art v 1 of SEQ ID NO:1. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. Further, it is noted that the proteins set forth in Appendix B of the declaration filed of Fatima Ferreira filed on 07/25/2008 were not isolated using IgE or serum of mugwort pollen allergic patients. Therefore, Applicant has not provided data to suggest that there are any other proteins of that size that are recognized by mugwort-pollen allergic patients as described in Katial et al. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument are not sufficient to overcome the rejection.

12. Claims 1, 4, 15 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Paulsen et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 03/11/2008.

Applicant's arguments and 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues:

"Applicants not only disagree with the Examiner's characterization of the prior art disclosures but also submit that the Examiner has erroneously placed the burden on Applicants to "prove" that the claimed allergen is distinct from the peptide of the prior art. Applicants reiterate that it is not their burden to demonstrate uniqueness but instead the Examiner's burden to demonstrate anticipation. Thus, it is improper to demand that Applicants "prove" that the various "approximately 40.9 kDa" mugwort pollen extracts of the prior art are different from that which is presently claimed, particularly when Applicants have previously presented ample evidence suggestive of distinction (e.g. differences in measurable parameters such as MW, pI, amino acid composition, etc.) and more recently accumulated evidence that casts doubt on the Examiner's suggestion that Applicants' SEQ ID NO: 1 is "more likely than not" to be among the mugwort pollen extracts identified in the prior art (see Appendix B of the attached declaration). Specifically, as the data provided herewith as Appendix B demonstrates, several potentially allergenic proteins within the range of 40-44 kDa band coexist in mugwort pollen extract.

As noted previously, the suggestion that a certain result or characteristic occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Likewise, the fact that an event ~ result from a given set of circumstances is not sufficient to establish anticipation. *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Under the principle of inherency, anticipation may not be established by probabilities or possibilities ("A prior art event cannot be established based on speculation, or where a doubt exists." *Ethyl Molded Product Co. v. Betts Package, Inc.,* 9 USPQ 2d 1001, 1032-33 (E.D.KY 1988). Rather, the doctrine of inherency is available only when the prior inherent event can be established with certainty. Thus, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Accordingly, when relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

In this case, Applicants previously presented evidence that the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. were not identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Applicants herewith present further evidence establishing that the reference proteins could be any one of a number of extract proteins (See Appendix B). Thus, Applicants respectfully submit that since one cannot be certain that the claimed peptide is necessarily present in any of the references, the references cannot anticipate the invention of the pending claims.

In sum, Applicants respectfully submit that none of the polypeptides described in the prior art are identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1. Since the cited prior art references fail to explicitly or inherently suggest each and every claimed element, Applicants submit that they cannot anticipate the invention of the pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the anticipation rejections of claim 1, 4, 15, 18, and 38 in view of the amendments and remarks herein. "

It remains the Examiner's position that Paulsen et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by gel permeation chromatography (In particular, Figure 6 A and B, approximately 45kDa fractions; 'Gel Permeation Chromatography' section on page 207; Table 1; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa fraction of Figure 6A and 6B in Paulsen et al. is the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant has not met their burden to show that the allergen in Paulsen et al. is not the allergen of SEQ ID NO:1 by saying that it is not necessarily the same allergen since it could have been any one of the allergens found in Appendix B submitted in the declaration of Fatima Ferreria on 07/25/2008. No sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6, but on the other hand no information has been provided to unequivocally prove that the isolated protein of Paulsen is not the recited

Art v 1 of SEQ ID NO:1. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. Further, it is noted that the proteins set forth in Appendix B of the declaration filed of Fatima Ferreira filed on 07/25/2008 were not isolated using IgE or serum of mugwort pollen allergic patients. Therefore, Applicant has not provided data to suggest that there are any other proteins of that size that are recognized by mugwort-pollen allergic patients as described in Paulsen et al. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument are not sufficient to overcome the rejection.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsen et al. (of record), Brandys et al. (of record), Hirschwehr et al. (of record), De La Hoz et al. (of record), Katial et al. (of record), **or** Paulsen et al. (of record) each as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) each in view of U.S. Patent 4,459,360 (of record) for the same reasons as set forth in the Office Action mailed on 03/11/20008.

Please note: The Office Actions mailed on 08/01/2007 and 03/11/2008 referred erroneously to claim 19 instead of claim 18 in this rejection that is directed to a kit. The Examiner apologizes for the inadvertent error and has corrected rejection, as set forth below.

Nilsen et al., Brandys et al., Hirschwehr et al., De La Hoz et al., Katial et al., and Paulsen et al. have been discussed previously (of record).

The claimed invention differs from the prior art by the recitation of a kit in claim 18.

U.S. Patent 4,459,360 (The '360 Patent) teaches the use of a diagnostic system for detecting the presence of IgE antibodies for allergy screening. Specifically, the '360 Patent teaches the use of mugwort allergens from Artemisia vulgaris pollen for use in a diagnostic test kit to screen liquid test samples for IgE (In particular, column 2, lines 24-41, column 5, line 15, and claim 6; whole document). The reference teaches that such a kit is an effective allergy screening system, especially useful for screening a large number of allergens at once, and is economical, simple to manufacture, and easy and inexpensive to analyze (In particular, column 8, lines 21-27).

It would have been obvious to one of ordinary skill in the art at the time of invention to use the isolated allergen fraction of Paulsen et al. or the isolated allergen band of Nilsen et al., Brandys et al., Hirschwehr et al., De La Hoz et al. or Katial et al. in a diagnostic kit for allergy screening for that allergen as taught by the '360 Patent because the '360 Patent teaches that such a kit would be economical, easy to analyze and useful as an allergy screening system.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Applicant's arguments and 1.132 declaration of Fatima Ferreira filed on 07/25/2008 have been fully considered, but are not found persuasive.

Applicant argues:

> "Applicants respectfully submit that US '360 fails to cure the above-noted deficiencies of the Nilsen et al., Brandys et al., Hirschwehr et al., De La Hoz et al., Katial et al., and Paulsen et al., namely the disclosure of an ~40.9 kDa Art v 6 protein defined in SEQ ID NO: 1. Thus, in that the prior art references, alone or in combination, fail to teach or suggest all the claim limitations, Applicants respectfully submit that the Examiner has failed to set forth a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection of claim 19 in view of the amendments and remarks herein.

It remains the Examiner's position that Nilsen et al., Brandys et al., Hirschwehr et al., De La Hoz et al. and Katial et al. teach the protein of SEQ ID NO:1 for the reasons set forth in the Office Action mailed on 03/11/2008 and *supra*. It also remains the Examiner's position that it would have been obvious to one of ordinary skill in the art at the time of invention to use the isolated allergen fraction of Paulsen et al. or the isolated allergen band of Nilsen et al., Brandys et al., Hirschwehr et al., De La Hoz et al. or Katial et al. in a diagnostic kit for allergy screening for that allergen as taught by the '360 Patent because

the '360 Patent teaches that such a kit would be economical, easy to analyze and useful as an allergy screening system.

15. Claims 39-40 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 29, 2008
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